Lung volume reduction surgery as salvage procedure after previous use of endobronchial valves

Caviezel, Claudio ; Guglielmetti, Laura-Chiara ; Ladan, Mateja ; Hansen, Henrik Jessen ; Perch, Michael ; Schneiter, Didier ; Weder, Walter ; Opitz, Isabelle ; Franzen, Daniel

Abstract: OBJECTIVES Lung volume reduction (LVR) is an efficient and approved treatment for selected emphysema patients. There is some evidence that repeated LVR surgery (LVRS) might be beneficial, but there are no current data on LVRS after unsuccessful bronchoscopic LVR (BLVR) with endobronchial valves (EBVs). We hypothesize good outcome of LVRS after BLVR with valves. METHODS In this study, we retrospectively investigated all patients who underwent LVRS between 2015 and 2019 at 2 centres after previous unsuccessful EBV treatment. They were further divided into subgroups with patients who never achieved the intended improvement after BLVR (primary failure) and patients whose benefit was fading over time due to the natural development of emphysema (secondary failure). Patients with severe air leak after BLVR and immediate concomitant LVRS and fistula closure thereafter were analysed separately. RESULTS A total of 38 patients were included. Of these, 19 patients had primary failure, 15 secondary failure and 4 were treated as an emergency due to severe air leak. At 3 months after LVRS, forced expiratory volume in 1 s had improved significantly by 12.5% ($P = 0.011$) and there was no 90-day mortality. Considering subgroups, patients with primary failure after BLVR seem to profit more than those with secondary failure. Patients with severe air leak after BLVR did not profit from fistula closure with concomitant LVRS. CONCLUSIONS LVRS after previous BLVR with EBVs can provide significant clinical improvement with low morbidity, although results might not be as good as after primary LVRS.

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Lung volume reduction surgery as salvage procedure after previous use of endobronchial valves

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Visual abstract

Key question: Is salvage lung volume reduction surgery (LVRS) reasonable after bronchoscopic lung volume reduction (BLVR) with valves?

Key findings: LVRS after BLVR with valves showed significant improvement of lung function with low morbidity and no mortality.

Take-home message: LVRS after previous BLVR with valves is reasonable at least as salvage procedure.

Central image

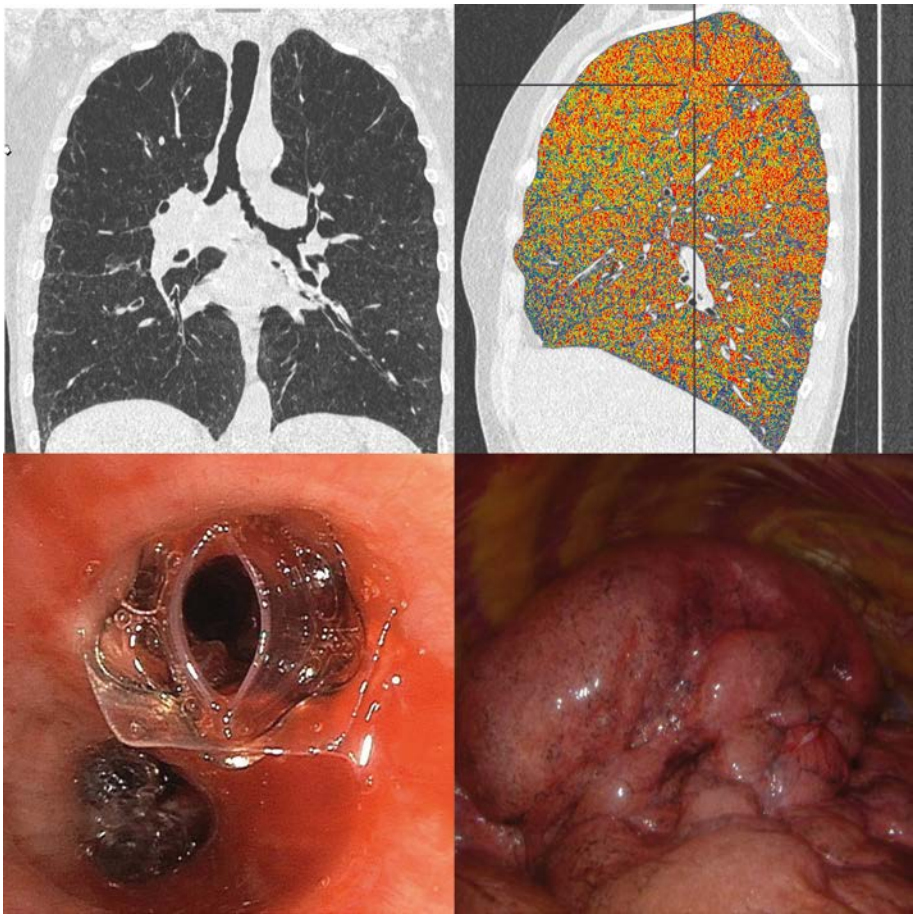

Figure legend for Central image:

Bilateral, upper-lobe predominant emphysema: coronal CT scan (left upper corner), sagittal densitometry of the right lung (right upper corner), endobronchial valve in situ (left lower corner), hyperinflated right upper lobe during thoracoscopy (right lower corner)

Abstract

Objectives:

Lung volume reduction is an efficient and approved treatment for selected emphysema patients. There is some evidence, that repeated LVR surgery (LVRS) might be beneficial, but there are no current data on LVRS after unsuccessful bronchoscopic LVR (BLVR) with endobronchial valves (EBVs). We hypothesize good outcome of LVRS after BLVR with valves.

Methods:

In this study, we retrospectively investigated all patients who underwent LVRS between 2015 and 2019 at two centers after previous unsuccessful EBV treatment. They were further devided into subgroups with patients who never achieved the intended improvement after BLVR (primary failure), and patients whose benefit was fading over time due to the natural development of emphysema (secondary failure). Patients with severe air leak after BLVR and immediate concomitant LVRS and fistula closure thereafter were analyzed separately.

Results:

A total of 38 patients were included. Of these, 19 patients had primary failure, 15 secondary failure and four were treated as an emergency due to severe air leak. At three months after LVRS, FEV1 had improved significantly by 12.5% (P=0.011) and there was no 90- day mortality. Considering subgroups, patients with primary failure after BLVR seem to profit more than those with secondary failure. Patients with severe air leak after BLVR did not profit from fistula closure with concomitant LVRS.

Conclusions:

LVRS after previous BLVR with EBVs can provide significant clinical improvement with low morbidity, although results might not be as good as after primary LVRS.

Key words:

LVRS, BLVR, lung volume reduction surgery, endobronchial valves, emphysema

Introduction

Lung volume reduction (LVR) has been established as a beneficial and safe procedure in patients with pulmonary emphysema and hyperinflation. Lung volume reduction surgery (LVRS) and bronchoscopic lung volume reduction (BLVR) with endobronchial valves (EBVs), coils or bronchial thermal vapor ablation (BTVA) are available (1-3). All methods have been demonstrated to improve lung function, exercise capacity and quality of life in patients with both heterogeneous and homogeneous emphysema (4-7). LVRS and BLVR with EBVs have both been shown to prolong survival in highly selected patients (7, 8). For selection of patients and the optimal LVR procedure, it is recommendable to establish multidisciplinary conferences (9, 10).

However, chronic obstructive pulmonary disease (COPD) is a progressive disease and neither LVR procedure is able to stop the natural course with an annual lung function decline and recurring hyperinflation (11). Therefore, initially successful LVR treatment effects may diminish over months or years (4, 12, 13). Repeated LVRS (Re-LVRS) shows promising results in highly selected patients, who are slowly deteriorating after initially successful LVRS (14, 15). Once a patient who already had LVR with EBVs is referred, LVRS might be offered.

To the best of our knowledge, there are so far no reports on LVRS after BLVR.

In this retrospective study from two European centers, we aimed to investigate LVRS after previous BLVR with EBVs with focus on mortality, morbidity and outcome.

Patients and Methods

Ethical approval

This study was performed under both institutional board's ethical approval.

All patients with previous BVLR with EBVs, who underwent LVRS at one of the two study centers (Department of Thoracic Surgery, University Hospital Zurich, Switzerland and

Department of Cardiothoracic Surgery, University Hospital Rigshospitalet, Copenhagen, Denmark) between December 2015 and December 2019, were included. Previous BLVR had been performed at the institutions or elsewhere. Repeated LVR were considered, when previous LVR was assessed to be unsuccessful (primary failure) according to the multidisciplinary emphysema board or initial benefit had faded over time (secondary failure). In- and exclusion criteria for LVRS were described previously (16, 17) and were similar in both study centers.

As many patients were referred from other centers, indications for EBV were not always according to our own policy and our usual emphysema board protocol. However, institutional guidelines from both study centers generally read as follows:

Primary scheduled for LVRS:

- bilateral, upper-lobe predominant emphysema
- bulleous or paraseptal emphysema
- concomitant nodule

Primary scheduled for BLVR with valves:

- heterogeneous emphysema markedly involving one whole lobe without collateral ventilation
- bilateral homogeneous emphysema without collateral ventilation

Absent collateral ventilation must be proven by a interlobar fissure integrity score > 85% (measured by StratX®, Pulmonx, USA) and a negative Chartis® measurement.

All patients – where both LVRS and BLVR are possible – are fully offered and explained all alternatives. However, many patients already have their own firm preference.

After LVRS, patients after previous BLVR were retrospectively allocated to two groups:

(1) Primary EBV non-responder (primary failure): no clinical improvement from beginning to three months after BLVR despite bronchoscopic revision attempt in case of absent target atelectasis (i.e. for valve re-placement);

(2) Secondary EBV non-responder (secondary failure): loss of benefit after initial subjective and objective improvement following BLVR (with and without target lobar atelectasis). The time interval between BLVR and the time of “secondary failure” was only driven by the patient’s decision to announce subjective loss of the initial benefit.

Patients with high-flow fistula after BLVR who thereafter received surgery for combined fistula closure and LVRS (during the same hospitalization), were analyzed separately.

Decisions to remove EBVs prior to LVRS depended on presence of target atelectasis (absent target lobe atelectasis triggered indication to remove EBVs, whereas left in place in case of evidence of atelectasis).

Surgery and perioperative phase

Preoperatively, all potential LVRS patients were functionally assessed with spirometry and bodyplethysmography. For cardiac evaluation, a transthoracic echocardiogram was performed for screening for pulmonaly hypertension. If systolic pulmonary arterial pressure, exceeds 35mmHg, patients are further assessed with right heart catheterization. If mean pulmonary pressure exceeds 35mmHg, they are usually excluded from LVRS.

LVRS target zones were selected by using CT scans, perfusions scans, densitometries and intraoperative emphysema appearance. The area with most destruction in heterogeneous emphysema was approached in cases without persisting atelectasis and without functional valves in situ, respectively. In patients with persistent atelecatasis and therefore valves left in situ, a target zone on the contralateral side was searched imperatively.

LVRS was performed by video-assisted thoracoscopic surgery (VATS) or exceptionally by anterolateral thoracotomy in case of severe pleural adhesions. Pulmonary resection was performed with standard staplers and 1-2 chest tubes were placed applying suction with 2 – 5 cm H20. All patients were extubated in the OR and transferred to intensive care or intermediate care units.

Follow-up and outcome measures

Follow-up of pulmonary function fests (PFTs) was scheduled at 3 months postoperatively.

Primary outcome measures were improvement of forced expiratory volume in first second (FEV1) and residual volume (RV). Secondary endpoints included length of hospital stay (LOS), chest tube time, postoperative complications and 90-day mortality.

Statistical analysis

Descriptive statistics were used to summarize patients' characteristics. Normality was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were reported as mean and standard deviation (SD) and compared using two-sample independent t-tests. Non-normally distributed continuous variables were reported as median and range and for comparisons between two groups the Mann Whitney U test was used. Paired continuous variables were compared using paired-samples t-test. Categorical variables were summarized as frequencies (%) and compared using Pearson's chi-squared test or Fisher's Exact test where applicable.

Results

Thirty-eight patients were included (figure 1). Four patients had persistent pneumothorax with high-flow fistula even after removal of EBVs. Nineteen patients were primary EBV non-responders despite previous bronchoscopic revision (group 1), and 15 patients had secondary failure (group 2). Both groups were further divided into subgroups dependent on the presence

of target atelectasis. Five patients were primary EBV non-responders despite the presence of a target atelectasis compared to 14 patients without atelectasis. In group 2, three patients had loss of effect despite a persistent atelectasis after initially successful EBV treatment, and 12 patients with both loss of effect and atelectasis. EBVs were removed prior to LVRS in all patients without evidence of atelectasis. In those with persistent atelectasis (n=8), EBVs were removed in three patients attributed to group 1. In patients with secondary failure and persistent atelectasis (n=3), EBVs were not removed and LVRS was performed contralateral.

LVRS outcome in patients with primary or secondary failure after previous EBVs (n=34)

Nineteen patients were female (55.9%). Thirty patients had a VATS procedure (88.24%), while four patients had VATS converted to a thoracotomy due to adhesions. Median LOS was 8 days (interquartile range (IQR) 6-13) . Median chest tube time was 5 days (IQR 3-11). Ten patients (29.4 %) had prolonged air leak longer than 7 days, and one patient had revision surgery for fistula closure (2.9%). One patient had a pneumothorax after chest tube removal and needed a new chest drain. No other relevant postoperative complications occurred. Ninety-day mortality after LVRS was zero.

Pre- and postoperative values of PFTs are displayed in Table 1. Median time interval between BLVR and LVRS was 10 months (IQR 6-14.25).

LVRS outcome comparing patients operated for primary failure (n=19) vs secondary failure (n=15)

There was no significant difference of LOS (9 versus 7 days), chest tube time (6 versus 4 days) and proportion of patients with prolonged air leak (43% versus 20%) between group 1 and 2. However, improvement of PFT values between pre- and post LVRS was more pronounced in group 1 (Table 2). Median time interval between BLVR and LVRS in patients with primary

failure (9 months, IQR 5-13) did not differ significantly from patients with secondary failure (median 12 months, IQR 7-16), p = 0.286.

LVRS outcome in patients treated with EBVs but without achieving a lobar atelectasis

Concerning patients with absent atelectasis, there were no significant differences in LOS, chest tube time, and proportion of prolonged air leak between the 14 patients with primary failure compared to the 12 patients in group 2. Again, improvement of PFT values was distinctly better in the primary failure group (Table 3). Median time interval between BLVR and LVRS in patients with primary failure (9 months, IQR 4.75-13.5) did not differ significantly from patients with secondary failure (11.5 months, IQR 6.25-15.75), p = 0.494.

LVRS outcome in patients with (persistent) lobar atelectasis after EBVs (primary or secondary failure, n=8)

There were eight patients with (persistent) atelectasis. Of these, EBVs were removed prior to LVRS in three patients, but in five patients EBVs were left in situ and LVRS was performed at the contralateral side. In all eight patients, there were no anaesthesiological or perioperative complications. Median LOS was six days (IQR 4-14 days) and a median chest tube time of three days (IQR 2-12 days). Three had a prolonged air leak (37.5%). At three months postoperatively, there was only a significant improvement of RV and RV/TLC, respectively, but not in FEV1 (Table 4). In patients who had EBVs removed before LVRS (n=3), median LOS was 15 days (range 6-20), and median chest tube time was 12 days (range 1-17). Two patients had a prolonged air leak. FEV1 improved from median 840 ml (540-1370) to 1140 ml (730-1550). Preoperative median RV was 3790 ml (value only known for n=1 patient), postoperative median RV was 3795 ml (range 2900-4690ml)..

In patients who did not have EBVs removed and received contralateral LVRS (n=5), median LOS was 5 days (range 2-11), and median chest tube time was 3 days (range 2-10). One

patient had a prolonged air leak FEV1 improved from median 785 ml (range 640-1190) to 880 ml (range 780-1120). RV decreased from median 4475 ml (range 4210-5450) to 3830 (3360-4890).

Median time interval between BLVR and LVRS was 11 months (IQR 8.25-14).

Outcome of patients with high-flow fistula (n=4)

Four patients with immediate pneumothorax after BLVR with EBVs developed a high-flow fistula. EBVs were removed during the same hospitalization (after a median of 11 days after BLVR, IQR 4.5-15.3), followed by VATS. All patients had a fistula at the non-target lobe, which was closed surgically. At the same time, LVRS was performed at the target lobe. Median postoperative LOS was 10.5 days (range 7 – 45). Median chest tube time was 19 days (range 2- 43) with one patient having a postoperative chest tube time of 43 days and a second patient of 30 days, respectively. One 63-year old female patient died because of suicide during in-patient rehabilitation two weeks after LVRS. One 58-year old male patient reported no benefit at three months postoperatively. Complete pre- and postoperative PFTs were only available in two patients. Mean FEV1 increased from 550 ml (± 210 ml)) to 700 ml (±141 ml) and RV increased from 5470ml (± 720) to 6070ml (± 1725ml). DLCO decreased from 25 % (±5%) predicted to 21 % (±5.8%) predicted.

Discussion

This retrospective study aimed at investigating the postoperative outcome of patients who underwent LVRS after previous BLVR who despite initial success deteriorated or who were unsuccessful immediately after EBV treatment.

LVRS in this sequence is not ideal and has to be considered as salvage therapy. Key issues of a successful LVRS includes many aspects but selecting the right volume and the right target area for resection in balance with physiologic parameters is of paramount importance. After

EBVs, a lobar atelectasis may be present and valves may be still in place causing disturbance of bronchial secret clearance. Both leads to compromises in LVRS treatment. Despite this, the presented data show that the procedure can be offered in some patients without ninety-day mortality and a significant improvement in lung function. This information is important for interdisciplinary emphysema-boards counseling patients. Patients must know, that LVRS after EBV might still be possible but is not equally effective than performed at first choice. The concept of LVRS and EBV are distinctly different despite the common goal of reducing hyperinflation of emphysematous lungs.

EBVs have been shown to be an effective and safe LVR procedure in several randomized controlled trials (6, 18-20). Improvement of FEV1 by 17% - 29.3% from baseline can be expected (5, 6, 18, 19, 21). Considering FEV1, there is a responder rate ranging between 47% at three months and 59% at six months (6, 18). There are several reasons for an unsuccessful EBV treatment, which can be classified as primary failure or as fading effect over time (secondary failure). While insufficient data is available on reasons for primary failure, there are several reported reasons for loss of efficacy over time. According to one-year follow-up data from the STELVIO trial, permanent removal of EBVs was required in 17% of the patients (22). Reasons included recurrent pneumothorax, torsion of bronchus, pneumonia, and granulation tissue. Besides other factors, the latter is maybe leading to paravalvular leakage and subsequent loss of atelectasis.

In both our study centers, patients who failed to develop an atelectasis or showed a loss of atelectasis after EBVs usually received revision bronchoscopy at one to three months after initial BLVR. Those who still had no profit despite of EBV replacement were discussed at the multidisciplinary emphysema board. Performing LVRS in some of these, there was a significant improvement of PFT values at three months, which was more distinct in patients with primary failure after EBV treatment. Furthermore, there is a tendency that patients, undergoing unplanned LVRS due to high-flow fistula after EBV treatment, might have a poor outcome.

Compared to primary LVRS with a reported improvement of FEV1 between 41% and 73% (23-26), efficiency of LVRS in patients with previous EBV therapy seems inferior. However, our study was not designed to answer this specific question, and comparison to historical LVRS cohorts is not without challenges. At least, postoperative morbidity and mortality seems comparable to primary LVRS.

Usually, target lobe atelectasis after EBVs is a good indicator for a favorable outcome with improvements of dyspnea, quality of life, 6-MWD and PFT values (27). However, in this study, we found eight patients with unsuccessful EBV treatment in spite of an existing target lobe atelectasis. Reasons for these rare cases are not completely understood. Certainly, indications for EBVs (in particular hyperinflation) must be reviewed. The question arises, if EBVs should be removed or left in situ prior to LVRS in these cases. Interestingly, all patients with persistent atelectasis but loss of clinical benefit from EBVs improved after LVRS in FEV1 and RV. According to our experience, these patients can be safely treated with contralateral LVRS, leaving EBVs in situ. Conceptually, this corresponds to results from previous studies concerning Re-LVRS, and as such, the fading benefit after EBVs reflects the natural course of pulmonary emphysema (11, 14, 28). The questions remains open, if valves should be removed prior to LVRS. A total lobar atelectasis is a relevant intervention into the physiology of a patient with advanced emphysema. Lobectomy performed during LVRS should be reserved only to the rare cases of a total lobar destruction. In all our cases, better preserved lung parenchyma was left in place. If valves would be removed and the totally atelectatic lung would re-expand including the functioning lung parenchyma, a more balanced remodeling by LVRS would be possible (29).

However, in patients with absent atelectasis, improvement was only significant in those with primary failure. This is surprising, since patients with secondary failure had experienced a temporary benefit after EBV treatment and thus, the principle of LVR was proven to succeed in these patients. Maybe in patients with secondary failure, the natural course of emphysema already was too advanced and prevented any LVR procedure to be beneficial again. According to our experience from this retrospective and heterogeneous data, EBV removal and

subsequent LVRS is a promising option in patients with primary failure after previous EBV therapy.

Time interval between BLVR and LVRS did not differ significantly between patients with primary failure and those with secondary failure. Only in patients with primary failure, the decision for a further intervention usually was already made three months after BLVR. In patients with secondary failure, this decision was dependent on patient's subjective loss of benefit. Altogether, including planning time for LVRS and several other patient factors, this finding might be coincidental.

Pneumothorax occurs in about 15-30% of patients after BLVR with EBVs, which is usually treated with a chest tube drainage (5, 18, 30). In almost 70% of cases, these patients have a prolonged air leak continuing longer than seven days (30). In our study, there were four patients with persistent high-flow fistula despite previous EBV removal, as recommended (2). In these patients, fistula closure by VATS followed by LVRS at the former EBV target lobe was performed. The outcome was poor. Although firm conclusions are not possible based on our small experience, combined fistula closure and LVRS might not be recommendable. Probably, a staged procedure is preferable.

There are some limitations to this study, essentially due to its retrospective nature and the relatively small and heterogeneous group of patients. Quality of EBV therapy was not assessed, and the definition of failure was not quantitative, thus, only assessed by patient's statements. Additionally, outcome of LVRS after EBV was only described by morbidity, mortality and PFTs, missing i.e. 6-MWD or quality of life. Maximum benefit after LVRS is usually reached after 3-6 months, whereas our data only consist of 3-month follow-up.

The small patient's number in this study might be sufficient to point out the favorable outcome of LVRS after previous EBVs, while the conclusions drawn from the subgroup analyses might be interpreted with some caution.

Conclusion

LVRS after previous BLVR with EBVs shows low morbidity, no mortality and significant clinical improvement can be expected, although results might not be as good as after primary LVRS.

Acknowledgement

None.

Funding

None.

Conflict of Interest

Daniel Franzen has received speaking honoraries and consultancy fees from Pulmonx SA. Walter Weder has received honoraries from Medtronic for teaching and proctoring. Henrik Jessen Hansen participates in advisory boards for Medtronic, BD/Bard and Medela. Michael Perch has recevided a research grant from PulmonX SA. All other authors declare no conflict of interest.

Author contribution

All authors fulfill the criteria for authorship according to the Contributor Roles Taxonomy (CRediT).

Figures

1: figure legend:

Figure 1: Flow chart of patients undergoing LVRS after previous BLVR using EBVs (n=38). BLVR, bronchoscopic lung volume reduction; LVRS, lung volume reduction surgery

Figure legend for Central image:

Bilateral, upper-lobe predominant emphysema: coronar CT scan (left upper corner), sagittal densitometry of the right lung (right upper corner), endobronchial valve in situ (left lower corner), hyperinflated right upper lobe during thoracoscopy (right lower corner)

Tables

Table 1

Mean (± SD)	pre-LVRS	3 months post LVRS	p-value
FEV1, ml	640 (± 210) (n=32)	720 (± 141.1)	**0.011**
FEV1, % predicted	23 (± 3.6) (n=34)	29.7 (± 6.4)	**0.010**
TLC, ml	7661.4 (± 1853.3) (n=26)	7599.6 (± 1782.8)	0.22
TLC, % predicted	137.4 (± 23.8) (n=27)	130 (± 18.0)	0.12
RV, ml	6070 (± 1725.3) (n=27)	5180 (± 720.2)	**0.014**
RV, % predicted	272 (± 80.6) (n=26)	238.7 (± 20.1)	**0.004**
RV/TLC	0.73 (± .011) (n=29)	0.70 (± 0.17)	**0.002**
DLCO, % predicted	25 (± 5) (n=34)	23.3 (± 5.8)	**0.043**

Table 1: Pulmonary function tests pre- and post-LVRS in patients with primary and secondary EBV failure (n=34). FEV1 = forced exspiratory volume in 1 second, TLC = total lung capacity, RV = residual volume, DLCO = diffusion capacity, ml = milliliter, SD = standard deviation

382 **Table 2**

	Primary failure (n = 19)			**Secondary failure (n=15)**		
Mean (± SD)	pre-LVRS	3 months post-LVRS	p-value	pre-LVRS	3 months post-LVRS	p-value
FEV1, ml	752.9 (± 303.9) (n=17)	871.9 (± 306.8) (n=16)	**0.003**	689.3 (± 220) (n=15)	733.9 (± 182) (n=13)	0.63
FEV1, % predicted	26 (± 8.4) (n=19)	31.3 (± 9.1) (n=17)	**0.002**	26.9 (± 11.6) (n=15)	28.9 (± 9.6) (n=13)	0.77
TLC, ml	8464.6 (± 1917.6) (n=14)	8334.3 (± 1879.6) (n=14)	0.39	6859.2 (± 1443.1) (n=13)	6742.5 (± 1248.9) (n=12)	0.21
TLC, % predicted	143.8 (± 25.1) (n=13)	136.7 (± 20.5) (n=14)	0.39	131.0 (± 21.4) (n=13)	122.3 (± 10.7) (n=12)	0.21
RV, ml	5144 (± 2437) (n=14)	4244.9 (± 2365.1) (n=14)	**0.035**	4812.3 (± 1263) (n=13)	4413.3 (± 1274.9) (n=12)	**0.020**
RV, % predicted	259.1 (± 57) (n=13)	227.2 (± 54.5) (n=14)	0.20	231.3 (± 43) (n=13)	207.8 (± 42.8) (n=12)	**0.021**
RV/TLC	0.70 (± 0.04) (n=16)	0.63 (± 0.06) (n=15)	**0.044**	0.69 (± 0.06) (n=13)	0.64 (± 0.07) (n=12)	0.062
DLCO, % predicted	31.22 (±12.12) (n=19)	36.2 (± 11.6) (n=16)	0.15	32.76 (± 12.31) (n=15)	32.4 (± 11.5) (n=11)	0.22

383

384 *Table 2: Pulmonary function tests in patients with primary failure (n=19) and in patients with secondary*
385 *failure (n=15). FEV1 = forced exspiratory volume in 1 second, TLC = total lung capacity, RV =*
386 *residual volume, DLCO = diffusion capacity, ml = milliliter, SD = standard deviation*

Table 3

	primary failure, no atelectasis (n = 14)			**secondary failure, never or loss of atelectasis (n=12)**		
Mean (± SD)	pre LVRS	3 months post LVRS	p-value	pre LVRS	3 months post LVRS	p-value
FEV1 ml	723.8 (± 291.6) (n=13)	827.7 (± 274.6) (n=13)	**0.045**	631.7 (± 180.2) (n=12)	678 (± 149.7) (n=10)	0.60
FEV1 %	26.1 (± 9.2) (n=14)	30.4 (± 9.7) (n=13)	**0.029**	25.6 (± 11.1) (n=12)	28 (± 9.3) (n=10)	0.74
TLC ml	8943.6 (± 1644.6) (n=12)	8785.5 (± 1674.1) (n=11)	0.42	6706.0 (± 1599.9) (n=10)	6694.0 (± 1299.2) (n=10)	0.37
TLC %	149.3 (± 23.3) (n=11)	143.1 (± 17.9) (n=11)	0.44	134.1 (± 23.0) (n=10)	123.3 (± 11.4) (n=10)	0.28
RV ml	5327.2 (± 2598.2) (n=12)	4364.4 (± 2653) (n=11)	**0.030**	4825 (± 1427.7) (n=10)	4471 (± 1354.4) (n=10)	0.084
RV %	271.3 (± 53) (n=11)	241.3 (± 50.7) (n=11)	0.20	236.5 (± 48.1) (n=10)	212.1 (± 45.5) (n=10)	0.08
RV/TLC	70.3 (± 4.2) (n=12)	65.1 (± 6.5) (n=11)	**0.15**	70.4 (± 6) (n=10)	65.7 (± 7.8) (n=10)	0.18
DLCO	30.6 (± 11.2) (n=14)	37 (± 12.4) (n=13)	**0.013**	29.4 (± 10.2) (n=12)	30.6 (± 11) (n=9)	0.18

Table 3: Pulmonary function tests in patients with primary failure and no atelectasis (n=14) and in patients with secondary failure and never or loss of atelectasis (n=12). FEV1 = forced exspiratory

volume in 1 second, TLC = total lung capacity, RV = residual volume, DLCO = diffusion capacity, ml = milliliter, SD = standard deviation

Table 4

Mean (± SD)	pre LVRS	3 months post LVRS	p-value
FEV1 ml	878.6 (± 300.1) (n=7)	990 (± 306) (n=6)	0.071
FEV1 %	28 (± 9.9) (n=8)	33.1 (± 8.8) (n=7)	0.12
TLC ml	6567.5 (± 1119.5) (n=5)	6330 (± 1282.5) (n=5)	0.24
TLC %	117.6 (± 9.2) (n=5)	114.7 (± 7.2) (n=5)	0.26
RV ml	4480 (± 622.7) (n=5)	3934 (± 850.7) (n=5)	**0.013**
RV %	205.3 (± 16.2) (n=5)	179.9 (± 28.8) (n=5)	**0.007**
RV/TLC	67.6 (± 5) (n=7)	58.4 (± 3) (n=6)	**0.004**
DLCO	37.9 (± 15.3) (n=8)	35.8 (± 9.8) (n=5)	0.54

Table 4: Pulmonary function tests in patients with (persistent) atelectasis after BLVR (primary or secondary failure, n=8).

FEV1 = forced exspiratory volume in 1 second, TLC = total lung capacity, RV = residual volume, DLCO = diffusion capacity, ml = milliliter, SD = standard deviation

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